BRITISH JOURNAL OF
TUBERCULOSIS
AND DISEASES OF THE CHEST

Vol. XLII. January, 1948 No. 1

# GENERAL ARTICLES

## SARCOIDOSIS*

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It is well known that three theories upon the etiology of sarcoidosis have been successively advanced. The tuberculous theory, the oldest one, was advanced by Besnier on the occasion of his first observations of lupus pernio, and later by Boeck dealing with sarcoids, and later still by Schaumann for lymphogranulomatosis benigna. A second theory, that the condition is leprous, has been advanced by South American dermatologists, especially Rabello; and a third, the belief that the condition is due to an autonomous virus.

### The Leprous Theory

I shall discard at once the leprous theory. It is easy to understand how Brazilian dermatologists should have thought of this possibility, when in later years they have found so frequently examples of tuberculoid lepra. Admittedly, there is an analogy between the histological structure of this tuberculoid lepra and of sarcoidosis. But this is not convincing evidence, because of the similarity in the tissue reactions which may occur from different agents. We are familiar, for instance, with the difficulties of histological diagnosis between tuberculosis and tertiary syphilis, and the tuberculoid reticulo-endothelial reaction may appear as a mode of defence resulting from a special allergic condition due to a variety of different infections. It is found, moreover, in leishmaniasis.

But the best argument, an irrefutable one, against the leprous theory is that even if this etiology can be considered for Brazilian cases, it is inconsistent that the same explanation can hold for European cases, which are common where leprosy does not occur.

### The Tuberculous Theory

Evidence for this view rests on probabilities and presumptions derived from the histological structure of the lesions, the existence of previous tuberculosis, the co-existence of other tuberculous manifestations, and the tuberculin

* A paper read to the Sections of Dermatology and Disorders of the Chest at the International Conference of Physicians in London, September 1947.

reaction; and from more direct evidence, the existence of tubercle bacilli in the lesions, the cultivation of tubercle bacilli from sarcoid tissues or the development of tuberculosis in experimentally inoculated animals. I propose to deal with the evidence bearing upon each of these in turn.

*Histological Structure.*—Sarcoid lesions, as is well known, are formed by masses of packed epithelioid cells with zones of lymphocytes and sometimes giant cells. But the time is past when these findings can be regarded as sufficient upon which to diagnose tuberculosis, because we know that tuberculoid leprosy, tertiary syphilis, and leishmaniasis all give similar pictures. On the other hand, it is possible to find, even in the more advanced lesions of sarcoidosis, islets of fibrinoid degeneration, but never zones of caseation which are almost a rule in old tuberculous foci. Moreover, the giant cells in sarcoidosis may simulate Langhans cells, though more frequently they are of plasmodial type with numerous nuclei scattered indiscriminately.

*The Existence of Previous Tuberculosis or Co-existence of Other Tuberculous Manifestations.*—The absence of previous tuberculosis impressed Schaumann from the start of his researches, and the association of sarcoidosis with active forms of tuberculosis in glands, bones, joints or skin is practically never seen.

The occurrence of sarcoidosis, however, in patients who have previously suffered from tuberculosis has been recorded. Desbucquois recently made an interesting observation on this point in a patient who had a primary tuberculous infection in 1932 with a positive tuberculin test. In 1942 she developed sarcoidosis with lesions of the skin, glands and lungs, when the tuberculin test became negative. Six months later, when these features were recessive, her tuberculin test became positive again.

Finally, patients suffering from sarcoidosis may afterwards develop genuine tuberculosis, involving the lungs, bones or other organs. In this event the tuberculin test becomes positive, while the sarcoid lesions gradually disappear. Such an association cannot be regarded as evidence for the tuberculous nature of sarcoidosis. The same thing is frequently seen in Hodgkin's disease, in which the two conditions may be seen side by side in related glands, though evidence of this kind in no way allows us to regard the two diseases as identical. But with sarcoidosis the association with tuberculosis seems not only to be very exceptional, but there is some mutual exclusion between the two. Supporters of the tuberculous theory think it is true that sarcoidosis can possibly be a stage of a benign pre-tuberculosis, and that evolution towards a definite tuberculosis is only the end of the first stage.

*The Tuberculin Reaction.*—Schaumann included in his definition of lymphogranulomatosis benigna of bovine tuberculous origin a negative tuberculin test which he considered to be a rule. I do not share this opinion, for, like Lomholt, I have found a third of these patients to show a positive test. Admittedly, the remaining two-thirds with the negative test exceed the expectation of a negative reaction among normal persons in adult life. The practical conclusion from this is that in dubious cases in which the diagnosis between tuberculosis and sarcoidosis is in doubt, especially in pulmonary forms, tuberculin energy should be regarded as important evidence in favour of sarcoidosis. Attempts to explain this anergy have been made by the theory of "procutins" and "anticutins," especially by Jadassohn, Martenstein, Loewenstein, and

Fallner—the one favouring, the other inhibiting, the tuberculin reaction. But the difficult thing in accepting this explanation for sarcoidosis is to account for a negative reaction produced by " anticutins," denoting thereby that such patients have shown no allergic reaction to tuberculosis, whereas the histological appearances of the lesions typify an allergic response.

During recent years the study of this tuberculin anergy has been reopened by vaccinations with B.C.G. of persons suffering from sarcoidosis. If there is an absolute anergy in a person uninfected by tuberculosis, such vaccination produces a positive cutaneous reaction; whereas, on the contrary, if there is a prevalent positive anergy in the course of a special form of tuberculosis, anergy remains complete. The evidence on this point in sarcoidosis is contradictory. Lemming found an absence of tuberculous allergy and claims to have produced local lesions showing the epithelioid structure of sarcoids by inoculation with B.C.G. On the contrary, Sohier and Gregoire found some evidence of tuberculous allergy. Clearly, this work requires repetition on a larger scale. Where a positive reaction to tuberculin occurs in sarcoidosis the reaction is always local and never focal in the lesions, indicating that the subject has previously been infected by the tubercle bacillus, but not that the skin lesions are of tuberculous nature.

There is, however, a further explanation for the negative tuberculin reaction: that an autonomous virus might be responsible. Partial anergies of this kind are known to occur in some physiological and infective conditions, and the possibility that it is an explanation in sarcoidosis is worth further consideration.

*Detection of Tubercle Bacilli by Culture and Inoculation.*—The skin lesions are the best material for these investigations. Although the majority of results have been negative so far, there are a number of positives. But when these are analysed they hardly stand critical examination. Some of them have been obtained on patients where the clinical diagnosis was not clear: in others a bacillus has been found and cultures and inoculations were negative. Sometimes a patient's lesions were definitely tuberculous, and sometimes positive inoculations have been obtained by subsequent recultures of the filterable virus form of tubercle bacillus, evidence for which is untrustworthy. It needs to be emphasised again that in order to prove the tuberculous nature of a disease the finding of acid-fast rods microscopically is not sufficient: the organism has to be cultured and identified, and its pathogenic action has to be demonstrated by inoculation.

I have never been able to obtain a positive inoculation from sarcoid tissue in any of the cases I have investigated personally. May I cite one case which allowed me to establish the identity of sarcoidosis and Heerfordt's syndrome. This was a most striking example of multiple recent fresh lesions, a confluent eruption of sarcoids over the whole body along with glandular enlargement and involvement of the lungs. One would have expected that if ever a positive result for the identification of the tubercle bacillus in sarcoidosis was to be obtained, this case should have been the ideal one. Twelve rabbits and guinea-pigs were inoculated in various sites—skin, muscle, anterior chamber of the eye and brain—and, in addition, blood from the patient was inoculated into the testis. Prolonged observation of these animals over several months failed

to show any evidence of tuberculosis, and the patient has recovered from his lesions spontaneously after several months. If this is tuberculosis, then it has to be regarded as quite a new form whose characteristics are fundamentally different from the ordinary forms.

Supporters of the tuberculous theory have made much of the case described by Kyrle, in which numerous tubercle bacilli were found scattered in a lymphocytic and histiocytic infiltration in a biopsy taken from sarcoid lesions only ten days old (an early date for a diagnosis). On the thirty-sixth day, however, biopsy showed the bacilli to have disappeared, and at the same time the infiltration had taken on an epithelioid type. On the ninety-fourth day the infiltration had completely disappeared. Both the precocity of the clinical diagnosis and the unusual speed with which the lesions resolved are striking features of this case. On the other hand, out of two guinea-pigs inoculated with blood from the patient, one died with tuberculosis. The evidence points to the fact that this patient had tuberculosis and was in a period of bacillæmia.

Believers in the tuberculous theory, and among them Warfvinge, have repeated this work and believe that tubercle bacilli can be found only during a short initial period and soon disappear as the lymphogranulomatous tissue develops. But if the organism is able to produce embolic lesions in the skin in this way, it must be assumed that the patient is already definitely tuberculous and in a state of bacillæmia. This seems quite extraordinary, since the lesions developed in such a torpid way. Warfvinge recalls, moreover, that the rat shows immunity towards classical tuberculosis, even high doses of tubercle bacilli producing only proliferative lesions in this species, epithelioid cells, without necrosis, but with or without giant cells. Kallos ascribed this property to a latent infection by *Bartonella auris rati* which infects laboratory rats, and considers that proliferation of macrophagic cells is responsible. He claims to have obtained classical tuberculosis with caseation after having previously cured a series of rats by means of arsenical and antimonial preparations, removing the spleen and blockading the reticulo-endothelial tissues with injections of Indian ink before inoculating tubercle bacilli intraperitoneally.

Such investigations give the impression that if sarcoidosis is supposed to be a special form of tuberculosis owing to an intense defence by the organism, proliferation of reticulo-endothelial tissues is responsible. Where this fails tuberculosis would resume its usual type.

Concerning the bacillus rather than the " soil " in relation to this view of the ætiology of sarcoidosis, Schaumann was able to isolate a tubercle bacillus from three of his cases—twice of the bovine variety, and once of the human. In a fourth case, where a gumma was present, he found a bovine bacillus. From the start of his investigations Schaumann gave particular attention to special corpuscles with a double contour, frequently present in the lymph nodes and the tonsils. Later on he found them in lupus vulgaris, tuberculosis verrucosa cutis and leprosy. Heidingsfeld found them in lupus erythematosis, and Nanta in the enlarged spleen of mycosis. Finally, Schaumann observed, emerging from these corpuscles, ramifying elements with divided or enlarged endings. Numerous authors have interpreted these as elastic fibres. Schaumann considers them as elements of the streptothrix type. Along with Hallberg, using a special staining technique with night blue, he found these present also

in tuberculosis and in sarcoidosis as well, and he concluded that they could be produced by genuine tuberculosis. Hollstrom, using Hallberg's staining method, with which numerous dermatophytes appear to be acid-fast, found in a sarcoid lymph gland ovoid corpuscles more or less acid-fast and a few acid-fast bacilli. Such investigations raised the problem of whether quite new forms of tubercle bacilli, having the morphology of streptotricheæ, played any part in the etiology of sarcoidosis. If so we are a long way from classical tuberculosis, and until bacteriologists have given more evidence of the nature of these corpuscles and their derivatives by means of cultivation, and proved their pathogenic power by inoculation of cultures, their importance remains undecided.

### The Theory of an Indeterminate Virus

This view has been advanced for a long time, especially by Danish authors —Kissmeyer, Jens Nielsen, and Lomholt—all of whom have abandoned the tuberculous theory. The opthalmologists are also inclined to accept the hypothesis of the specific virus advanced by Menil and Oaks for Heerfordt's syndrome. The idea of a specific virus as a cause of sarcoidosis has been taken up again in recent years by Kveim, who prepared an antigen from sarcoid tissues, preferably lymph nodes, and obtained positive intradermal reactions in cases of sarcoidosis but no reactions in cases of tuberculosis of the skin. Whether this reaction is specific requires discussion; contradictory results have been published. Niels Danbolt believes in its value and has observed a sarcoid-like structure at the site of the reaction. He thinks that it is particularly of value for the diagnosis of internal lesions and that, as it is positive in sarcoids only and negative in lupus and tuberculoids, it points to Boeck's sarcoidosis as a disease *sui generis*.

On the contrary, Lomholt found Kveim's reaction neither constant nor reliable. He emphasised the delay in the reaction, which sometimes occurs as late as the eighteenth month after injection. Moreover, he has found a positive result in lupus vulgaris, and at the site of injection has noticed ulcerations and indurations remaining for two years. He stressed the slowness of the reaction, its dangers and its questionable specificity.

Putkossen found Kveim's reaction strongly positive in one case of lupus pernio and stated that antigen can be prepared not only from sarcoid tissues, but from tuberculous lymph nodes and leukæmic lymph nodes. Probably the reaction cannot be ascribed to the presence of a specific microbe, patients with sarcoidosis reacting by a sarcoid pattern towards various antigens. It is impossible so far to make definite conclusions. Is it possible to assume that a reaction appearing several weeks or months after the introduction of the antigen really shows an allergic state towards the injected antigen? Nothing of this kind is known for all other antigens so far. On the other hand, the reaction, once produced, may remain for several months and show an epithelioid structure. Inoculation of B.C.G. may produce the same manifestation, and it seems well established that patients suffering from sarcoidosis have a special capacity for a reaction of the reticulo-endothelial type. Extensive further investigations with controls using the intradermal introduction of other substances are necessary.

## Conclusions

From what has been said it can be seen how difficult it is at present to decide between the two views of the etiology of sarcoidosis: whether it is tuberculous or due to an autonomous virus. The experimental evidence is at present conflicting.

Hypothetically, several authors, especially Alfred Bermann, are prepared to accept the view that Boeck's disease is a genuine tuberculosis, modified by special reactions on the part of the organism, reactions deriving from a constitutional factor. Conceivably this might be a mutation of reactions of a race which has long been subject to tuberculosis, in which the less resistant hosts have been diminished by death and more and more of the survivors would tend to suffer from the sarcoid type of disease. Although this is a stimulating hypothesis, there is not the slightest evidence for it so far. From the clinical point of view sarcoid disease is certainly not diminishing, and the tuberculous theory becomes more and more difficult to accept for all cases we are observing. What a strange tuberculosis that invades lungs, lymph nodes, bones, parotid gland, the eye, cranial nerves and brain, without resulting in caseation, without bacilli, giving negative inoculations in animals and recovering spontaneously! I have already said, and should like to repeat, that if this is tuberculosis, then it is quite a new form, of which we cannot at present understand the first principles.

One of the main clinical arguments against the tuberculous hypothesis is to be found in children who already show the multifarious manifestations of the disease. Ought these to be considered as evidence of a primary tuberculous infection? It is inconsistent with our experience to assume that young children react in this way to a recent tuberculosis. Should one consider that they have inherited a new type of reaction to the disease? All this seems indefensible. The argument against a tuberculous etiology is a strong one against which it seems very difficult to advance objection.

Returning to the hypothesis of an unknown virus, my own feeling, after having been a supporter of the tuberculous theory, is again to reconsider this hypothesis willingly. Nevertheless, we cannot hide its weaknesses, and one has to admit that there is not the slightest evidence for it at present. On the other hand, we have the same difficulty with other diseases, among them the whole series of granulomatoses, especially Hodgkin's disease. Paul Courmont, Gaté and Gardere, who studied one case thoroughly, thought they had found evidence for a special virus, polymorphous, difficult to cultivate, giving micro-cultures of acid-fast and alcohol-fast bacilli, or granulous non-acid-fast bacilli. This organism seems to be a close relative of the tubercle bacilli and Hensen's bacillus.

Several writers have regarded sarcoidosis as a syndrome disease, produced sometimes by the tubercle bacillus, human or bovine, sometimes by Hensen's bacillus, and sometimes by an autonomous virus. The etiology being manifold, such an eclectic theory is only a " solution de facilité." Sarcoidosis clinically has all the characteristics of an autonomous disease, a morbid entity, and not a single monomorphic tissue reaction elicited by different causes.

Thus the question of the etiology remains unsettled. Investigations will need to be conducted with method and patience, and one should refrain from hasty conclusions from uncertain facts.

My own studies and experiments have covered some thirteen years, and though one may feel that one knows the disease from the clinical and pathological point of view, the etiology is still a baffling problem. Questions which one had thought were settled recurrently prove still to be undecided, and one is constantly aware of the small extent of our knowledge of sarcoidosis compared with what remains to be discovered.

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# ON THE KVEIM REACTION IN BOECK'S DISEASE*

By Prof. H. HAXTHAUSEN

From the University of Copenhagen

Boeck's disease is one of the subjects most frequently discussed by dermatological congresses—in particular, of course, at the Scandinavian meetings, where it is one of the few topics able to set the usually cool Scandinavian temperament aflame. Naturally the cause of this great interest in Boeck's disease lies in the many puzzling features of the lesion, especially the still unsolved problem: Is this lesion a particular form of tuberculosis or is it a specific disease *per se*?

In the discussion of this in recent years the so-called *Kveim reaction* has played a conspicuous rôle; and as this reaction has been tried out particularly in the Scandinavian countries, while it appears to be known but little outside these countries, I found it rather natural to select this subject for my paper.

In 1941 Kveim[1] in Norway showed that it is possible in patients suffering from Boeck's disease to produce a characteristic and fairly specific local reaction by intracutaneous injection of a special antigen. This antigen consists in a suspension of the granulation tissue characteristic of the disease. As a rule the suspension is made by grinding an affected lymph gland in saline. The suspension is sterilised by brief heating to 60° C. for two hours twice at intervals of twenty-four hours, and it is injected intracutaneously in various dilutions—in a dose of 0·1 c.c.—just as in a Mantoux test. During the following days, at the site of the injection there appears merely an uncharacteristic redness or, at the most, a very slight infiltration which soon disappears again. It is only after a latent period of one to two weeks—and sometimes considerably longer—that there appears on the site of injection a small papule, which slowly increases in size and gradually is transformed into a small nodule. Sometimes this nodule shows evidence of central necrosis—and in some cases it even may undergo ulceration—persisting now for many months without extending farther. Subsequently, it always disappears again, though often this takes one to two years. Histological examinations of such positive reactions have shown them to be of a

* A paper read to the Sections of Dermatology and Disorders of the Chest at the International Conference of Physicians in London, September 1947.

structure quite resembling the morbid changes produced in the skin by the disease itself.

At present we do not know with certainty how the appearance of the positive reaction is to be explained, but the most obvious possibility appears to be that here we are dealing with a specific allergic reaction, even though it has to be admitted at once that on several points it deviates from the allergic skin reactions we otherwise are acquainted with.

As to its specificity, from the findings reported by Kveim himself and subsequently by Danbolt,[2,3] Danbolt and Wisloff Nilssen,[4] Putkonen,[5] Lomholt[6] and others it is evident that the reaction is positive in nearly all cases of Boeck's disease—also in cases where the skin is not affected—while it is positive in other diseases but quite exceptionally. It is of particular interest that the reaction nearly always has been negative in lupus vulgaris and other forms of tuberculosis of the skin. In specificity, then, this test comes fully up to, or even higher than, several other intracutaneous reactions of definite allergic nature.

According to more recent studies carried out by Danbolt,[7] the active factor in this reaction is connected with the cellular elements in the suspension, but hitherto it has not been practicable with certainty to extract it or to define its chemical character in detail. It is rather thermostable, as its action is not quite abolished by autoclaving for a fairly short time, though weakened somewhat.

In control experiments with the so-called Frei antigen, which is prepared indeed in a similar manner from lymph glands from patients with lymphogranuloma inguinale, Kveim always found a negative reaction in cases of Boeck's disease. On the other hand, Lomholt has seen positive reactions on employment of an antigen made of lymph glands from a patient with lymphatic leukæmia; and various other observations of at any rate apparently positive reactions have been reported with other antigens.

The most interesting findings in this respect have been reported by Swedish investigators, who, on employment of tubercle bacilli as antigen, were able to obtain positive reactions in a number of cases of Boeck's disease. Thus Lemming[8] has been able by Calmette vaccination to produce some changes which histologically quite resemble those observed in Boeck's disease. Furthermore, by intracutaneous injection of killed tubercle bacilli Warfvinge[9] has produced reactions that appeared after the same latent period as the Kveim reaction, persisted very long and showed quite similar histological features.

Naturally the fact that tubercle bacilli—living or killed—are able to induce a reaction which at any rate greatly resembles the Kveim reaction has been taken as substantial evidence by the authors who look upon Boeck's disease as a particular form of tuberculosis, basing their view especially on the pioneering works of Schaumann. Still these studies furnish no decisive proof of a tuberculous etiology.

If the active principle of the Kveim antigen really be tubercle bacilli or products of such bacilli, they will have to be present in the tissue attacked in Boeck's disease. A priori, I think, this may not be excluded decidedly, but it is safe to say that the tubercle bacilli then at any rate are capable of hiding very well.

As a matter of fact, Björnstad[10] has recently reported some observations

which detract somewhat from the evidence furnished by the Swedish experiments. For he showed that intracutaneous injection of killed tubercle bacilli also is able to produce a Kveim-like reaction in normal individuals who are tuberculin-negative. In contrast hereto, the Kveim antigen proper has no such effect. So considering the fact that patients suffering from Boeck's disease as a rule are tuberculin-negative, this implies in itself an explanation of the reaction to killed tubercle bacilli, and thus it is by no means necessary to assume the pre-existence of a tuberculous infection.

Björnstad's experiments show clearly that the Kveim antigen is not identical with the tubercle bacillus antigen. When, nevertheless, both kinds of antigen are able in Boeck's disease to produce reactions of the same character this may be due, for instance, to the circumstance of certain decisive partial antigens being common to the two antigens. But it is also possible that the explanation has to be looked for in other circumstances, and that the Kveim reaction is to be considered under some angle other than the specific allergic.

Really it is rather difficult to look upon the Kveim reaction as a specific allergic phenomenon. It has been mentioned already that several different antigens are able in Boeck's disease to produce a positive reaction. Furthermore, in its histological structure and in its very protracted course, the reaction deviates from all other allergic skin reactions known so far. While, for instance, in the trichophytin or in the Frei reaction we meet with a papular infiltration that appears within a few days and disappears again rather rapidly, it takes the Kveim reaction one to two weeks or longer to make its appearance and some additional weeks to attain the fully developed nodular stage, and finally it takes one to two years to subside completely. While other allergic skin reactions histologically as a rule show the ordinary features of chronic inflammatory processes, in the Kveim reaction we meet with the same typical granulation tissue as is encountered in Boeck's disease. It may aptly be said that the reaction imitates the skin eruptions of the disease itself.

We know of no other allergic reaction completely analogous to these features, but in this connection it still is to be mentioned that, among others, Sulzberger[11] sometimes has found a tuberculin reaction to take a very protracted course, with a tissue reaction of typical tuberculoid structure—that is, features still of a similar nature to the Kveim reaction.

Considering the difficulties encountered when we try to fit the picture of this reaction in the frame of allergy—which otherwise indeed is large as well as elastic—it is only natural that we have looked about for some other possible explanation.

One of the possibilities I wish to point out is that here we might be faced by the phenomenon which has been designated as "isomorphic reaction." This, as you know, means that various irritants applied to an area of normal skin may locally produce eruption of a lesion found elsewhere on the skin. This is known, especially from cases of psoriasis, in particular as the so-called Köbner scratch phenomenon, but it is encountered also in a great many other lesions—*e.g.*, lichen planus and certain syphilitic eruptions. The fact that the positive Kveim reaction in Boeck's disease completely resembles eruptions of the lesion itself is quite in keeping with the assumption of an

" isomorphic reaction." On looking further into the matter, however, we meet with difficulties here too.

While, for instance, in psoriasis numerous different irritants of mechanical, chemical or other nature are able to provoke eruption of the disease, so far in Boeck's disease it has been possible to produce a positive reaction with only a few, though different, antigens—namely, besides the Kveim antigen proper, also antigen made of leukæmic lymph nodes and antigen in the form of killed tubercle bacilli. Danbolt has made experiments with catgut sutures in the skin and other unspecific measures causing an inflammatory process—all with negative results. I have made some experiments with intracutaneous injection of aleuronat and talcum suspensions, which produced a local, rather protracted, inflammatory process. But this reaction took the same course in the controls and in a patient with Boeck's disease, who gave a fine positive reaction to the original Kveim antigen just as the unspecific reactions were about to fade—after about two weeks.

If the Kveim reaction is a form of " isomorphic reaction " we have to assume then that only very few irritants are able to produce it.

The circumstance that the Kveim reaction is elicited by only a few of the antigens tried hitherto does not rule out the possibility that it may be an " isomorphic reaction." But it is not to be denied that a number of facts go against this hypothesis. Thus, if it were a matter of true provocation of the disease we would expect that once the reaction was induced it would spread at any rate sometimes and persist like the spontaneous eruptions. No such spreading is seen, however, and the reaction always subsides, albeit most slowly, even though the spontaneous eruptions present remain unchanged.

Some observations which also are rather incompatible with the assumption of an " isomorphic reaction " have been reported by Lomholt. By employment of the Kveim antigen in a number of cases of Boeck's disease Lomholt obtained reactions which not only were very strong but also in their course presented a picture entirely different from the usual. These reactions made their appearance after a very long latent period—sometimes several months—and after the nodular stage was reached there appeared some deep ulcerations that healed but slowly. Some of these ulcerations persisted for years, and in some cases their recurrence was even observed after extirpation of the skin area attacked. It is obvious that such reactions, which are of a character entirely different from that of the disease itself, may hardly be interpreted as " isomorphic."

On summing up the observations made with the Kveim reaction it may be said that for entirely practical diagnostic purposes it means a new and valuable adjuvant. Regardless of the mechanism of the reaction, it has proved nearly always to be positive in Boeck's disease and negative in other cases. Thus it meets all reasonable requirements of specificity. It will prove particularly useful in cases without any skin eruption and, on the whole, in cases where the clinical features are indistinct. Its diagnostic value is greatly limited by the fact, however, that the reaction develops so slowly, in some cases appearing only after some weeks or even months. Furthermore, the disagreeable reactions observed by Lombolt naturally require some caution in its employment.

As to the pathogenesis of the reaction we are still in the dark. Some fea-

tures are suggestive of an " isomorphic reaction," whereas other and, I think, stronger arguments speak in favour of a specific allergic reaction. But even if we accept the allergic hypothesis it still remains an open question whether the antigen is specific of Boeck's disease or whether it is derived from some product of the tubercle bacillus. It is at this point, I think, that future investigations ought to aim primarily. Thus it ought to be investigated systematically whether antigen prepared from unquestionably tuberculous lymph glands gives a similar reaction as does the original Kveim antigen. Further comparative studies ought to be carried out with the Kveim antigen and with antigen of tubercle bacilli in an extensive biological and clinical try-out.

The Kveim reaction has not yet settled the old controversial question whether Boeck's disease is a disease *per se* or merely a special form of tuberculosis. On the contrary, the interesting information furnished by this reaction so far has kindled the zest of the advocates of both theories. But the reaction implies a great possibility of approaching the actual state of the matter through further studies. Until the outcome of such new investigations is available I shall at any rate refrain from taking part in the controversy concerning the etiology of this puzzling disease. As yet we are wanting really decisive facts in this respect, and the sober attitude to this problem must be the same now as before—namely, wait and see.

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# SARCOID*


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THE subject of my paper is the much-disputed ætiology of sarcoid. The controversy about it arose because sarcoid has certain features which make a tuberculous origin acceptable, while others seem to make it highly improbable.

The links with tuberculosis can be summed up as follows:

1. The occasional co-existence of sarcoid and tuberculosis.
2. The occasional alternation between sarcoid and tuberculous manifestations.

* A paper read to the Sections of Dermatology and Disorders of the Chest at the International Conference of Physicians in London, September 1947.

3. The rare but well-documented cases in which sarcoid lesions of skin were transformed *in situ* into lupus, and vice versa.
4. The termination of sarcoid by tuberculosis as shown by autopsy. Pinner and Rubin recently reviewed these cases and showed that their number was not negligible.

Those who dispute the tuberculous origin admit that in a number of cases links between the two diseases exist, but deny that they prove a tuberculous origin. In their opinion they could be explained by assuming that sarcoid patients may be more susceptible to an infection by Koch's bacillus, and, conversely, tuberculosis may pave the way for the causative agent of sarcoid, which may be a virus.

But their chief argument is that sarcoid has certain constant or almost constant features which do not occur in classical tuberculosis. These are:

1. The histological picture.
2. The negative tuberculin reaction.
3. The absence of tubercle bacilli.

For the study of the histological picture of sarcoid in general, and that of its relation to tuberculosis in particular, the skin offers very good opportunities, for we are guided by the clinical appearance and can easily check up by repeated biopsies.

My own material consists of over thirty cases of sarcoid, and several hundred of tuberculosis of skin. I wish to express my grateful thanks to all my colleagues who, over a period of nearly fifteen years, sent me their biopsy material and in many cases also their patients for examination.

A fully developed sarcoid lesion (Fig. 1) shows sharply demarcated round or oval or irregularly shaped foci, consisting of epithelioid cells, with no, or very little, inflammatory reaction around. Caseation is absent. With certain modifications, which we shall discuss later, this rather simple picture is found again and again, which makes the diagnosis "sarcoid tissue" easy. Yet sarcoid tissue is not confined to Besnier-Boeck-Schaumann sarcoid. It would be strange if it were so. The body has only a few ways of reacting to damaging agents, the number of which is practically unlimited. Sarcoid tissue is also very frequently seen in leprosy and rarely in other chronic granulomas, including syphilis and leishmaniasis. From the purely histological point of view we can only state a sarcoid-type reaction; it needs further clinical, bacteriological and other data to corroborate the diagnosis of Besnier-Boeck-Schaumann sarcoid.

Does the histological picture suggest any relation to tuberculosis? At first sight, certainly not; it seems to be entirely different from the caseating tubercle with its giant cells, epithelioid cells and the strong inflammatory reaction of the classical tuberculosis. Yet closer examination of a large material shows that certain modifications in the sarcoid tissue may appear that make a relation less unlikely.

One or several giant cells may be seen. Fig. 2 shows a typical Langhans giant cell in sarcoid tissue. In other instances sarcoid may contain in some parts a distinct inflammatory component. Fig. 3 shows in the uppermost part

# PLATE I.

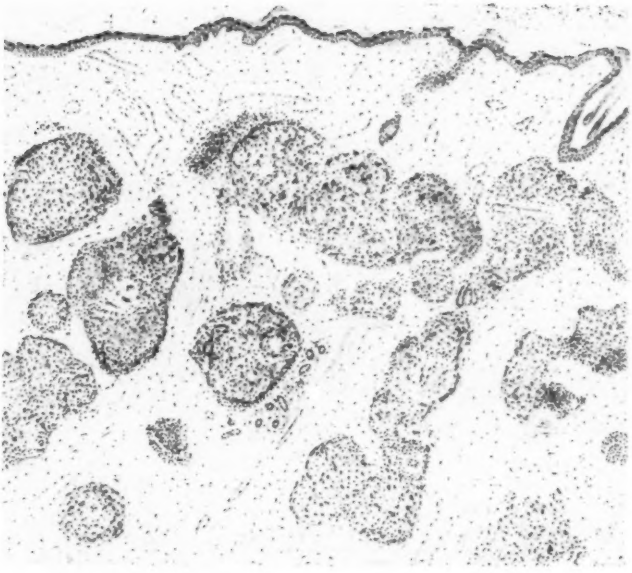

FIG. 1.—SHARPLY DEFINED ROUND OR OVAL OR IRREGULARLY SHAPED ISLANDS CONSISTING OF EPITHELIOID CELLS, WITH NO OR VERY LITTLE INFLAMMATORY REACTION AROUND. (F. LEWANDOWSKY.)

A

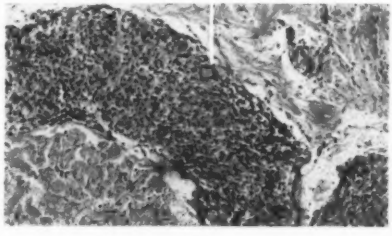

FIG. 2.—SARCOID TISSUE, CONTAINING A LANGHANS GIANT CELL (A). (× 80.)

To face p. 12

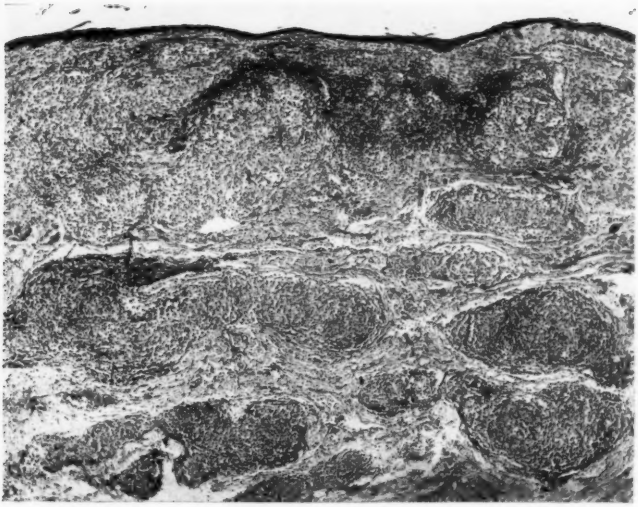

FIG. 3.—FAIRLY STRONG LYMPHOCYTIC REACTION IN THE UPPERMOST PART OF THE CUTIS. IN THE OTHER PART OF THE CUTIS NUMEROUS EPITHELIOID CELL ISLANDS WITH NO OR VERY LITTLE LYMPHOCYTIC INFILTRATE. (×38.)

FIG. 4.—STRANDS AND ISLANDS OF SARCOID TISSUE WITH A MODERATE LYMPHOCYTIC REACTION IN THE MIDDLE AND AT THE BOTTOM OF THE PICTURE. (×75.)

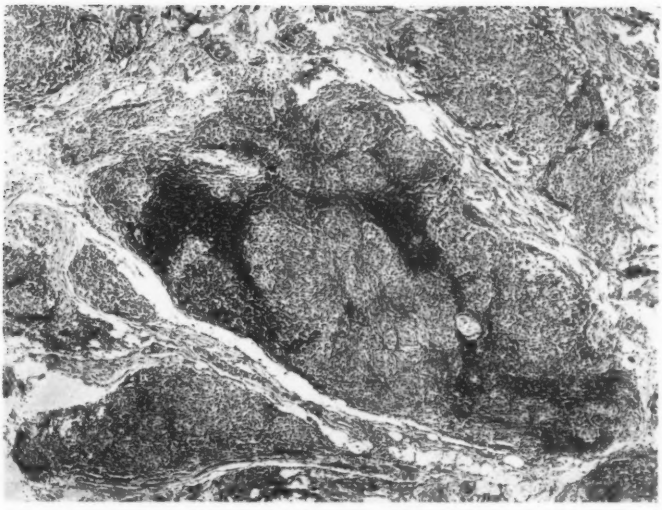

FIG. 5.—STRONG LYMPHOCYTIC INFILTRATION IN THE LARGE CENTRAL SARCOID FOCUS. SMALLER FOCI WITH NO OR VERY LITTLE LYMPHOCYTIC REACTION. (× 160.)

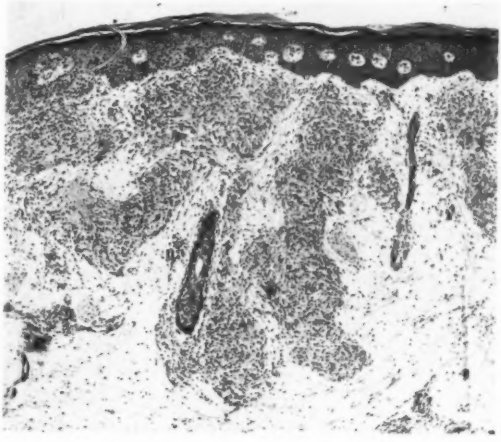

FIG. 6.—CLINICALLY LUPUS, HISTOLOGICALLY SARCOID-LIKE STRUCTURE. EPITHELIOID CELL STRANDS AND ISLANDS, HARDLY ANY LYMPHOCYTIC REACTION. (× 70.)

# PLATE IV.

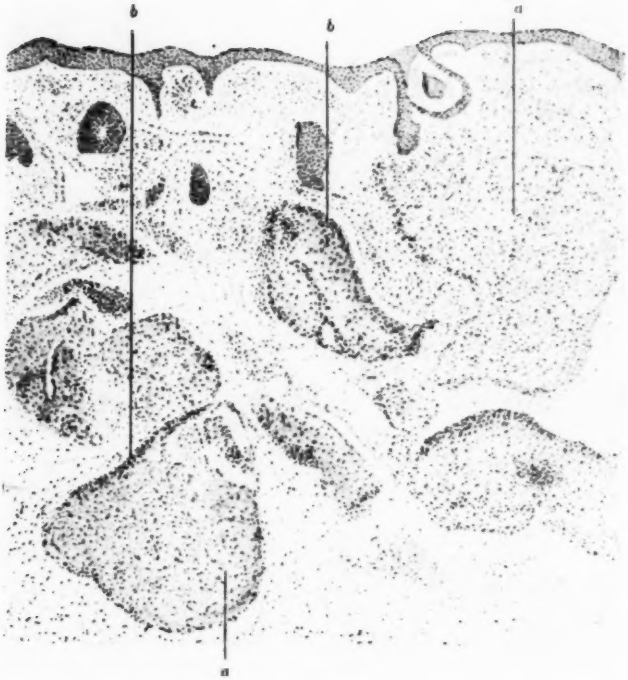


FIG. 7.—CLINICALLY LUPUS, HISTOLOGICALLY SARCOID-LIKE STRUCTURE. EPITHELIOID CELL ISLANDS (*a*); NARROW LYMPHOCYTIC BORDER (*b*). (F. LEWANDOWSKY.)

To face p. 13

of the cutis a fairly strong diffuse lymphocytic reaction. In the other parts of the cutis numerous islands of sarcoid tissue are seen with no or very little lymphocytic infiltrate. Fig. 4 shows strands and round foci of sarcoid tissue with a moderate lymphocytic reaction in the middle and at the bottom of the picture. In Fig. 5 the lymphocytic infiltration is stronger and in places begins to obscure the sarcoid structure. Surrounding the large focus are smaller sarcoid foci with hardly any lymphocytic reaction.

I should like to mention that in no instance did I find caseation in skin sarcoid, but it must be remembered that, except in the rare lupus miliaris faciei, caseation practically never occurs in tuberculosis of skin, especially in lupus. In addition, when examining serial sections of lupus nodules I found that, while the bulk of the nodule consisted of typical lupus tissue, sometimes one or two tubercles consisted of epithelioid cells only, with no or little infiltration around them, thus showing a sarcoid structure.

Recently an untreated lupus nodule was sent to me that, to my surprise, on histological examination proved to consist almost entirely of sarcoid tissue (Fig. 6). The biopsy was sent to me by Dr. Dowling and Dr. MacRae, taken from one of the lupus cases that they had chosen for calciferol treatment. On my enquiry Dr. MacRae confirmed that the case was a typical lupus in every respect, including a strongly positive tuberculin reaction, and that there was nothing to suggest the presence of sarcoid. The only other case of this kind that I could find in the literature is the one described by Lewandowsky and depicted in his classical work on tuberculosis of the skin. You see a reproduction of this picture in Fig. 7. Cases like these, where a lupus consists entirely of sarcoid tissue, are exceptional; but, on close examination, a small to moderate amount of sarcoid tissue in lupus is seen not infrequently. I should put it in my material at about 15 to 20 per cent. Even more frequently some lupus features are seen in sarcoid (about 25 to 30 per cent. of my material). I should also like to mention that some sarcoid tissue was formed almost regularly in lupus during its course of treatment with calciferol. Dr. Dowling and Dr. MacRae made biopsies at frequent intervals which they very kindly sent me for examination, and I was able to demonstrate them at this year's meeting of the British Association of Dermatology in Leeds.* In the discussion, Professor Miescher, Zürich, confirmed my findings in his own material.

We may conclude that sarcoid and lupus tissue are not as different as appears at first sight; in fact, the two conditions are linked together more closely histologically than they are clinically. I think one is entitled to say that the histological picture of sarcoid is not incompatible with a tuberculous origin.

Perhaps the most disputed feature in sarcoidosis of skin and the inner organs is the negative, or almost negative, tuberculin reaction in a very high percentage (about 80 per cent.) of the patients. At first sight a negative tuberculin test hardly seems compatible with an active tuberculous process and is, if I am not mistaken, the main reason why physicians are reluctant to think of sarcoid as a form of tuberculosis.

We are acquainted with a negative tuberculin test under the following circumstances:

* A report will be published in *Brit. J. Dermat.*, in 1948.

1. In persons who never had tuberculosis. This cannot be applied to sarcoid patients, some of whom had classical tuberculosis before or during their sarcoidosis.
2. In tuberculosis of the cachectic; hardly applicable to sarcoid patients who, on the whole, are in a fairly good general health.
3. The tuberculin test becoming negative during infectious diseases such as scarlatina, and especially measles. In scarlatina the tuberculin reaction, according to Lenneberg, is usually only weakened and reappears in full strength after five to ten days; in measles, according to Pirquet's investigations, the positive reaction reappears on the sixth, seventh or eighth day after the onset of the eruption. This is also quite different from the persistent negative reaction in sarcoid.

When J. Jadassohn, more than thirty years ago, found the negative tuberculin reaction in many sarcoid patients, he suggested that this kind of tuberculin anergy was of an entirely different nature from that of the other three well-known groups. In these the negative reaction was due to a lack or temporary exhaustion of the defence mechanism; in sarcoid, in his opinion, it was due to a defence mechanism of such perfection that the injected tuberculin was immediately dissolved and neutralised at the site of the injection, without battle, without any signs of œdema, exudate or inflammation. He assumed that this was caused by a specific substance circulating in the blood; hence his term specific or positive anergy. At that time, in 1914, this was a daring hypothesis, as hardly anything was known to support it. Since then certain experiments have been carried out, the results of which seem to be in favour of his interpretation. Even so, wrote Lemming of Stockholm as recently as 1940, " his theory has not received the attention it deserves, probably because it breaks with long-established opinions, and upon first acquaintance seems somewhat of a paradox."

The basis for a revision of our views on the interpretation of a negative tuberculin reaction has been provided by the experimental work of Rich and McCordock, Willis, and others. They showed that in a variety of conditions allergy does not run parallel with immunity, as one was accustomed to believe.

Pursuing this line of thought, Duprez of Brussels, in 1934, injected into normal (non-tuberculous) guinea-pigs a large number of small doses of tuberculin. The tuberculin reaction first became strongly positive, then gradually weaker, and finally in most animals completely negative. He then injected a large dose of very virulent tubercle bacilli which ordinarily would have killed a guinea-pig within a few days. He found, however, that they were in a state of complete immunity. No reaction, neither general nor local at the site of the inoculation, was seen in these tuberculin-negative animals. It seems to me more than likely that their negative tuberculin reaction was not the expression of a lack or an exhaustion of the defence mechanism, but that their defence mechanism was of such perfection that the virulent bacilli were neutralised, dissolved and made innocuous without any visible signs of a battle; their negative tuberculin reaction was in the nature of J. Jadassohn's specific or positive anergy.

Rothschild and co-workers made a similar experiment on tuberculous guinea-

pigs; after repeated tuberculin injections they became tuberculin-negative. Yet this did not deprive the animals of any aspects of their immunity; their resistance to a super-infection was equal or even superior to that of non-injected tuberculin-positive controls. The lesions in the tuberculin-negative animals consisted of epithelioid cell tissue, a fact only briefly mentioned in their paper. I think this is more than a coincidence and has a bearing on the sarcoid problem.

In sarcoid itself Lemming tested the nature of the negative tuberculin reaction by giving sarcoid patients repeated injections of Calmette's B.C.G. vaccine, containing living bovine tubercle bacilli of low virulence, which in other persons almost regularly produces a positive tuberculin test. In most of the sarcoid patients the tuberculin reaction remained negative. Lemming sees in this a strong indication that their body, in accordance with J. Jadassohn's positive anergy, contains a specific substance which neutralised the B.C.G. vaccine.

Numerous attempts have been made to demonstrate this substance in the serum of sarcoid patients, but the results differ. Martenstein, W. Jadassohn and others found it; Hämel, Pinner, Leitner and others failed to do so. Dr. Mills Hall drew my attention to work carried out by Wells and Wylie at the Sir William Dunn School of Pathology at Oxford. These authors in a personal communication informed me that they had found in sarcoid serum a property that actively neutralises tuberculin; their paper will be published at a later date.

Animal pathology makes a valuable contribution to our problem by showing that a striking analogy exists between sarcoid in man and tuberculosis, spontaneous as well as inoculated, in certain animal species. Gloyne and Page, W. Jadassohn and others showed that rats inoculated with tubercle bacilli respond by the formation of epithelioid cell tissue; their tuberculin reaction remains negative. Spontaneous tuberculosis in dogs, cats, horses and foxes shows, according to Nieberle, chiefly epithelioid cell tissue. In 33 to 40 per cent. of tuberculous dogs the tuberculin reaction was negative (Gerlach); little is known about the tuberculin reaction in the other animal species.

To sum up, the negative tuberculin test in sarcoid can no longer be considered as incompatible with its tuberculous origin, and thereby the second argument becomes invalid.

There remains the third argument: the absence of tubercle bacilli in the great majority of cases. However, during the last ten years positive results have markedly increased; they now number about twenty-six cases, in fifteen of which bacilli were found in the skin, chiefly by culture. Some of the positive cases are open to criticism, but there still remain a good number of fully established positive results, amounting to about 8 per cent. of the published cases that were investigated. These cases can hardly all be explained by human error, or by latent tubercle bacilli accidentally found.

As to the numerous negative cases, it should be remembered that in the whole group of tuberculides which are caused by hæmatogenous dissemination of bacilli in the skin we are very frequently unable to show the bacilli by any method. There is good reason to believe that in tuberculides as well as in sarcoid, bacilli can be demonstrated only at the earliest stage of the lesion; very

soon they disappear or, more likely, become altered in such a way as to defy our present methods.

This conference offers an opportunity to appeal to all physicians who meet a fresh case of sarcoid or fresh lesions, particularly skin lesions, in an old case to seek the co-operation of a bacteriologist without delay. In this way, I hope, the ætiology of sarcoid will be established beyond doubt at an early date.

It probably will be a much more arduous task to find out why certain people should respond to an infection by the tubercle bacillus with a sarcoid and not a classical tuberculosis. Schaumann believes that it is due to an attenuated bacillus of the bovine variety. I have given his arguments the careful attention they deserve, but must admit they did not entirely convince me. The sarcoid response to tubercle bacilli in a variety of animal species makes one think that we have to look for an unknown factor in the patients themselves. As far as I can see this problem is still unsolved. The other question as to whether the peculiar features of sarcoid—namely, the histology, the negative tuberculin reaction and the absence of tubercle bacilli in the great majority of cases—are compatible with a tuberculous ætiology can, in my opinion, be answered in the affirmative.

Finally, there is the marked improvement under vitamin D (calciferol) treatment in sarcoid that speaks in favour of its tuberculous origin. It may be argued that calciferol has not been tried out sufficiently in conditions other than tuberculosis, also that its action is still little understood. But whatever view we may take, whether we believe in the tuberculous origin of sarcoid or not, I am sure our feelings of gratitude to Charpy and to Dowling, who inaugurated this treatment, will be shared by all alike.

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# SCROTAL PNEUMOCELE AND INGUINAL HERNIA COMPLICATING PNEUMOPERITONEUM THERAPY

By M. M. NAGLEY

From Baguley Sanatorium

Although artificial pneumoperitoneum, at least in America, is coming into disrepute as a line of collapse therapy in the treatment of pulmonary tuberculosis—*vide* Pinner (1946) and Rafferty (1945)—it is the general impression in this country that, although the indications for its induction are diminishing, the measure has a place in treatment. In view of this it has been thought worth while to draw attention, following the paper of Rogers and Garrett (1947), to an interesting group of complications which may occur during the treatment.

## Review of Literature

Klopstock and Scheuler (1933), working purely on intestinal tuberculosis, first noted emphysema of the omentum as an accidental occurrence in pneumoperitoneum refills and demonstrated this fluoroscopically, Besta (1934) was apparently the first to observe " an elastic swelling of the scrotum " after 300 c.c. of oxygen and ascertained that the gas lay in the processus vaginalis and not in the subcutaneous tissues. Bennett (1938) reported the appearance of an inguinal hernia during pneumoperitoneum treatment and Rilance and Warring (1941 and 1944), in a now classic series of papers, mention the filling of an already existing small inguinal sac with fluid in a patient undergoing pneumoperitoneum injections. Daniels and Eisele (1938) also report an increase in scrotal size due to air under similar circumstances. Monto and Bradford (1943) describe scrotal pneumocele controllable partially by a pad.

Banyai (1946), reviewing the literature, mentions one case of scrotal pneumocele, three cases of umbilical pneumocele, and one case of hernia through the left lumbar triangle of Petit among his own patients.

The case recorded by Rogers and Garrett in the last issue of this journal is the first case in the British literature.

The following cases—three of scrotal pneumocele and one (in a female) of inguinal hernia—occurring during pneumoperitoneum treatment were all seen at the same sanatorium as the case of Rogers and Garrett, and are thought worthy of publication in order to determine whether other workers in the field have had similar experiences and in order to assess the significance of the phenomenon.

## Case Records

Case No. 1.—G. N., aged 21, a private, was admitted to the Military Wing of Baguley Sanatorium on September 3, 1947, with a history of heavy cough and sputum for eight months, night sweats for one month, and slight blood staining of the sputum on several occasions in mid-August. Pulmonary tuberculosis was diagnosed on the finding of a positive sputum, the clinical history and radiological evidence of a cavity in the subapical region of the right lower lobe.

General condition was quite good, afebrile, weight 11 st. 1 lb., B.S.R. 33 mm. in one hour (Westergren).

On September 15, 1947, a right phrenic crush was carried out under local anæsthesia and a pneumoperitoneum induced on September 23, 1947. Subsequent X-ray films have shown a good hemidiaphragmatic rise with definite contraction of the cavity, but at no time, even immediately after injection of 1,000 c.c. of air, has this air been demonstrated below the diaphragm.

On September 24, 1947, he developed slight pain in the right scrotal sac and a large scrotal pneumocele (right) was seen. The scrotum was rested on an elastoplast pad; the condition became less painful and tender and had completely subsided in exactly twenty-four hours.

This case showed several interesting characteristics:

1. Although many refills have been given since, there has been no recurrence of the scrotal condition.
2. At no time was there any surgical emphysema.
3. The patient had had a left orchidectomy as an infant.

The question of congenital small bilateral inguinal herniæ here cannot be excluded and would be an irresistible explanation of the scrotal pneumocele.

Case No. 2.—P. G., aged 18, a private, was admitted under the writer's care on March 31, 1947, with a history of hæmoptysis earlier in the year and cough and sputum for three months. On admission general condition was poor. sputum T.B. positive, B.S.R. 16 mm. in one hour, and there was radiological evidence of bilateral cavitated pulmonary tuberculosis more on the right. He was placed on strict bed rest and, on May 13, 1947, a pneumoperitoneum was induced. Between that time and July 15, 1947, when the P.P. was abandoned, improvement was made in the general condition and much healing occurred at both bases.

On July 16, 1947, a right artificial pneumothorax was induced, followed, on August 25, 1947, by a right thoracoscopy, when indivisible adhesions of the symphysis type were found and the A.P., in view of this and in view of X-ray evidence of extension of the disease in the right upper lobe, was abandoned.

There was subsequent gross deterioration of the condition clinically and radiologically, culminating on September 5, 1947, in recurrent large hæmoptyses. An emergency phrenic crush was performed followed by a large intraperitoneal injection of 2,000 c.c. of air, and two days later by a further 1,000 c.c. Bleeding ceased and the general condition improved markedly, but on September 8, 1947, three days after the emergency phrenic crush and P.P., a small, slightly painful left scrotal pneumocele developed. Apart from this being a psychological disturbance to a patient in extremis, no ill-result attended, and the swelling subsided in eight hours and weekly refills were continued. No recurrence of the condition was ever noted and the patient made a good clinical recovery from the emergency for which his pneumoperitoneum was re-induced.

The interesting feature here was that between May 13, 1947, and July 15, 1947, when his original pneumoperitoneum was in progress, no scrotal pneumocele occurred, but at no time during that period was any refill greater than 900 c.c. given.

Case No. 3.—A. N., aged 30, a fusilier, was admitted to the Military Wing of Baguley Sanatorium on February 3, 1947, with a diagnosis of pulmonary tuberculosis since November, 1946. General condition was good, sputum T.B. positive, weight 8 st. 8 lb., history of cough, early morning sputum, night

sweats and loss of flesh since September, 1946, B.S.R. 68 mm. in one hour. He was given preliminary treatment by strict bed rest on evacuation to this country from Italy in January, 1947, and a left phrenic crush was carried out on January 15, 1947, followed by a pneumoperitoneum on January 18, 1947. The radiological picture at that time was of left upper zone old infiltration and right mid-zone infiltration with commencing cavitation.

On admission to Baguley the pneumoperitoneum was thought to be ineffective, but before the final decision was made to abandon this form of treatment a routine refill was given on February 6, 1947, of 1,000 c.c. as previously. Four hours later the patient complained of right scrotal discomfort and on examination a right scrotal pneumocele was diagnosed. This subsided in twenty-four hours and caused no further trouble. There was no evidence whatever of surgical emphysema and radioscopy showed quite definite intraperitoneal air after the refill.

An interesting later finding in this case was that after abandonment of the P.P. in favour of a right A.P. the scrotal swelling recurred immediately following thorascopic division of adhesions, but this cannot be considered as statistically relevant, since some thoracic and abdominal surgical emphysema was present.

Case No. 4.—E. G., aged 29, a housewife, was admitted to Baguley Sanatorium on May 20, 1943, when the radiological appearance was of heavy infiltration over the entire left lung field with commencing cavitation in the mid and lower zones surrounded by much mottling especially in the supradiaphragmatic area on the left and minimal discrete nodulation of the right apex. The sputum was T.B. positive, the weight 7 st. 1 lb. (normal weight 11 st.), the general condition very toxic.

She was placed on strict bed rest, given a course of aurotherapy and considered for collapse therapy at a later date.

On April 13, 1944, a left artificial pneumothorax was unsuccessfully attempted and a pneumoperitoneum with 1,000 c.c. of air was induced, and a left phrenic crush performed. Weekly refills continued until July 8, 1944, when the patient complained of a lump in the right inguinal fold and an obvious inguinal hernia was seen. Screening showed a good left hemidiaphragmatic rise and much air below the diaphragm. The right inguinal hernia was obviously increasing in size with subsequent refills of 1,000 c.c., so that on July 27, 1944, the patient was transferred for repair of the hernia and the pneumoperitoneum temporarily abandoned.

At the operation on August 2, 1944, the usual type of inguinal hernial sac was found, distended to a small degree by a loop of small intestine, but to a much greater degree by intraperitoneal air which was evacuated, with complete reduction on screening of the subdiaphragmatic air. The patient made an uneventful recovery from the herniorrhaphy and on resuming the pneumoperitoneum refills there was no recurrence of the hernia.

In this case, however, the pneumoperitoneum lasted only for two refills after the operation and was abandoned in favour of a left thoracoplasty.

## Summary

1. Three cases of scrotal pneumocele and one case of inguinal hernia during artificial pneumoperitoneum therapy have been described.

2. In only one of these cases was the phenomenon associated with induction (Case 1). In another (Case 2) it was associated with a larger than normal air

injection, and in another (Case 4) with a larger than normal volume for induction purposes. In Case 3 it was apparently of incidental occurrence.

3. In agreement with Rogers and Garrett the writer has found that scrotal pneumocele is transient and does not necessarily indicate abandonment of the treatment.

4. While it is impossible in such a short series and by the very nature of the condition to state dogmatically that scrotal pneumocele and inguinal hernia occurring during pneumoperitoneum therapy is the enlargement of a previously existing embryological remnant of the processus vaginalis, one of the cases (Case 1) had a contralateral congenital hernia, and it is felt that all patients upon whom pneumoperitoneum induction is contemplated should be examined carefully for hernia as a preliminary measure.

I wish to thank Colonel Austin, A.D.M.S., North-West District, and Dr. H. G. Trayer, for permission to publish this paper; Dr. W. N. Rogers, my predecessor, for originally calling my attention to this work; and Dr. A. J. Coello for the kind loan of some notes of Case 4 and for his most helpful advice on the subject.

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# REVIEWS OF BOOKS

*Bovine Tuberculosis.* By JOHN FRANCIS. Staples Press, London. Price 25s.

In his introduction the author states that this volume is an attempt " to bring together all the important information on incidence, the development of the disease in the animal body, the mechanism of spread from one animal to another and the methods of control most likely to be successful, particularly in Great Britain." In this aim Mr. Francis has achieved a large measure of success, and the book is a very full review of our knowledge of the present time.

The evidence for the respiratory route of infection in animals is most convincingly presented and affords satisfactory scientific reasons for the well-recognised practical observation that the health of dairy herds is greatly improved when they are managed on the outdoor " bail " system introduced into this country by Mr. Hosier.

The essential difference between the almost invariably progressive primary complex in the bovine as opposed to the predominantly healing type of primary complex in the human is well stressed. Thus it is shown that the positive skin reaction in the dairy cow is a much more reliable index of progressive tuber-

culosis than the positive Mantoux in the human. This is a point of great significance, as it makes schemes for the eradication of bovine tuberculosis based on the disposal of the positive reactor economically possible. The evidence adduced in this book shows quite clearly that the eradication of tuberculosis from dairy cattle is now possible, and that its great prevalence at this time is a reflection on the social conscience of the country rather than the skill of the veterinary surgeon.

Most of the book is an analysis of morbid anatomical data obtained from many thousands of post-mortem examinations. This work is, on the whole, satisfactory and convincing. The bacteriological side is far less satisfactory. It leaves the rôle of infection of cattle by *M. tuberculosis* of the avian type quite unsolved. It is true that there are accounts of the avian type of bacilli having been isolated at post-mortem on cattle dying with progressive tuberculous lesions. The bacteriological criteria upon which this typing was based are not given, and hence the reported finding of the avian type in progressive lesions must be regarded with suspicion. This is particularly important in view of the very frequently observed fact that positive reaction of the avian type of tuberculin is frequent where cattle are kept in close association with infected poultry. It is clear that this question of avian infection of cattle is insufficiently understood and should be investigated afresh.

A valid criticism of the whole book could be made on the grounds that there is over-condensation of the vast number of papers which the author has consulted. This unfortunately makes the book somewhat difficult to read in places, but was probably imposed on the author by difficulty of paper shortage and publishing costs.

J. W. C.

*Tuberculosis and Chest Disease for Nurses.* By G. S. Erwin. J. and A. Churchill, London. Price 10s. 6d.

Three-quarters of this book are devoted to the various manifestations of tuberculous infection and one-quarter to non-tuberculous pulmonary diseases. Pulmonary tuberculosis occupies pride of place and is dealt with from all its aspects from prevention, through initial infection, course and complications, home and institutional management, etc., to final arrest or death. The author presupposes an elementary knowledge of respiratory anatomy and physiology in the reader, but has been careful to maintain a correct balance between the academic and more practical aspects of the subject. In this he has succeeded admirably, with a result that the intelligent nurse can readily understand the reasons behind the various forms of treatment which she, as an essential member of the therapeutic team, is helping to carry out. Theory is kept to a minimum, while practical nursing problems are stressed throughout. The simple style, liberal use of italics and subtitles, together with clear illustrations, combine to make a most readable book. With a minimum of mental effort, those engaged in this sphere of nursing will find most of their questions answered therein and it can with confidence be recommended to them.

F. H. S.

*The Nursing of Tuberculosis.* By O. V. Buxton and P. M. Maculloch Mackay. John Wright, Bristol. Price 7s. 6d.

This small volume contains the main essentials required by those engaged in the nursing of tuberculous patients, more especially during the institutional part of treatment. The early chapters on etiology, morbid anatomy and

respiratory physiology, etc., are advisedly brief, but it is difficult to see why the management of tuberculosis in pregnancy should occupy almost a third of the chapter devoted to etiology. The common forms of collapse therapy are outlined with some of their indications, but the importance of the presence of cavitation in a decision whether or not to employ collapse measures is not mentioned. Even with limited space available it is felt that a diagram of at least one type of A-P apparatus should have been included, if necessary at the expense of the rather inadequate illustration of the "structure of a tubercle." Similarly, among the special tests, some reference to the examination of the gastric contents for tubercle bacilli could well have replaced the description of the various colours which may be imparted to urine by certain drugs. As a handbook, however, it will be found a useful introduction for student nurses commencing training in this sphere, or for rapid revision for those about to take the Certificate of the Tuberculosis Association. F. H. S.

*Pathological Histology.* By ROBERTSON F. OGILVIE. Third Edition. E. and S. Livingstone, Edinburgh. Price 37s. 6d.

This book is designed to direct the attention of both the undergraduate and graduate medical student to the essential microscopical features of a section of diseased tissue. It is intended to be complementary to the microscope, the slides and the standard pathology textbooks; it replaces neither the standard textbooks nor the examination of the actual tissue sections.

The preparation of this new edition has resulted in the addition of forty-seven pages of text and twenty-six entirely new coloured microphotographs. Many of the previous microphotographs have been replaced by improved examples. The subject matter of the book is arranged in two sections, the first section referring to general pathology and the second to diseases of special organs. The subject is treated descriptively and very little reference is made to items of differential histological diagnosis. The text is concise yet lucid, and describes both the macroscopical and microscopical features of each subject, and in many places includes notes on etiological and clinical matters. This comprehensive discourse in the text is particularly welcome in that it emphasises the enormous importance in pathology of the correlation of the gross pathological features with the minute, and both of these features with those observed at the bedside. In places the conciseness of the text results in some dogmatism, this being well demonstrated in the discussion of the pilonidal sinus. An important feature of the book is the collection of coloured microphotographs. Such coloured illustrations have the great advantage of showing specific staining reactions and emphasising the general tissue pattern of the section. The majority of the illustrations in this book clearly demonstrate these advantages, although some show a rather wide variation in colour with the same staining combination and some show a confusingly similar tissue pattern; both of these faults are well demonstrated in the illustrations of the spindle-cell and fibro-sarcoma. A disadvantage with such illustrations is the frequently poor reproduction of cellular detail, and care must be taken not to illustrate ambiguous pictures requiring cellular detail for differentiation, this mistake being made in the illustration of an intraduct carcinoma of the breast which equally well might have been labelled as an example of simple hyperplastic disease. Such an error might merely represent a faulty caption to the illustration, another bad caption being that of Fig. 90, where one might search in vain for the supported cells.

This book, as a whole, is well produced and should assist students of pathological histology to learn their subject with greater interest, perhaps with greater ease and certainly with greater wisdom. A. B. H.

*The Child's Lung.* By S. ENGEL. Edward Arnold, London. Price 40s.

This book is concerned with the morphology of the lung from birth to adult life. From a vast amount of work, involving particularly three-dimensional reconstructions from serial sections of lung tissue, the author builds up a picture of the growing respiratory system.

The clinical application of this detailed study is made clear as each of the elements which go to make up the lung is considered. Thus, a most careful description of the lymph glands in relation to the trachea and bronchi is followed by a chapter on the hilum, including its radiological appearance at different ages, and an account of the response of these lymph glands to the primary tuberculous infection.

The author is, of course, using a tongue which is foreign to him, and, while in general his meaning is clear, there are occasions on which a recasting of his sentences would have made for easier reading. Devoted as it is to the description of original investigations and to deductions made from them, there is much in the book that will provoke disagreement. Both from this point of view and as a supplement to Miller's well-known book it is worth the attention of the physician interested in chest disease.

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## NOTICE OF MEETING
## JOINT TUBERCULOSIS COUNCIL

AT the last meeting of the Joint Tuberculosis Council, a new committee was set up to consider and report on the problem of tuberculous patients whose duties bring them into close touch with children. The convener of the new committee is Dr. Wilfrid Sheldon.

The report made by the Council's Nursing Committee dealing with the recent report of a Working Party on the Recruitment and Training of Nurses was ordered to be sent to the Ministries of Health and Labour and to the Department of Health for Scotland. The Joint Tuberculosis Council are greatly concerned about the absence from the Working Party's report of special provision for tuberculosis nurses. The publications of the Council on the problems peculiar to this type of nursing do not seem to have been brought to the Working Party's attention. The Joint Tuberculosis Council decided to ask the Ministry of Health to meet their representatives to discuss the matter.

The recent cuts in priority milk for tuberculous persons were discussed by the Council, and the Secretary was asked to inform the Ministries of Health and Food that the cuts were regarded with grave misgivings. In the Joint Tuberculosis Council's opinion the amounts of food available for tuberculous persons at home and in sanatoria are at dangerously low levels. The Council further decided to forward to the Ministries information concerning the dietary requirements of sanatorium patients compared with general hospital patients.

Another matter which received attention was the eligibility of tuberculous persons for supplementary financial assistance under the National Assistance

Bill. The Council endorsed the opinion of the Tuberculosis Group of the Society of Medical Officers of Health that eligibility for such aid should be based strictly on need and not necessarily on the fact that employment had been given up. The Secretary was instructed to convey this view to the Ministry of Health and to ask for some further information.

With the support of the Tuberculosis Association, the Joint Tuberculosis Council at this meeting authorised an approach to be made to the Ministry of Health for the publication of tuberculosis notification data, similar in form to the mortality statistics published by the Registrar General in his quarterly returns.

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## PAPWORTH VILLAGE SETTLEMENT, CAMBRIDGE

THE Libarrian is anxious to obtain (for binding) copies of the BRITISH JOURNAL OF TUBERCULOSIS for January 1940 and January 1941, and would gladly receive or purchase these from any reader having copies available and to spare.